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WITH ABSTRACT OF THE LITERATURE

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The Rôle of Punctate Basophilia in the Control of Industrial Plumbism

Quantitative Measurements of the Inhalation, Retention, and Exhalation of Dusts and Fumes by Man: II. Concentrations below 50 Mg. per Cubic Meter

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THE JOURNAL OF INDUSTRIAL HYGIENE

VOLUME XIII OCTOBER, 1931 NUMBER 8

A NIGHT INDUSTRIAL DENTAL CLINIC IN MONTREAL*

R. VANCE WARD, M.D., AND FRANK G. PEDLEY, M.D.

Montreal, Canada

IN 1927 and in the two subsequent years a considerable expansion in medical service in industry took place in the city of Montreal. Several industries which had no medical supervision whatever established health services run on modern lines, and others which had been doing some such work expanded their services to include active preventive medical work by a physician.

In a short time it was clear from the records of preemployment and periodic physical examinations that the incidence of all other minor remediable defects was completely overshadowed by the number of cases of dental caries. Scarcely a person was found who did not need some dental attention, and the condition of many mouths could be described as nothing less than deplorable.

The industries concerned were anxious to implement their medical services with some sort of dental care, but many difficulties stood in the way. The establishment of a dental clinic even of one chair is an expensive procedure from the standpoint of capital outlay. Dental work done in the factory takes a considerable amount of time away from the working day of the employee treated, and an investigation at first hand of the success of various industrial dental services in large plants in the northeastern part of the United States was not particularly encouraging. A few plants reported that the services were highly valued by the employees and were busy all the time; some reported rather indifferent success; and others had been closed up entirely.

The establishment of a dental clinic which would surmount all these difficulties and objections was the task undertaken by the Industrial Clinic at the Montreal General Hospital in 1928, and the result of this work was the clinic whose organization is outlined in this article.

The clinic was designed primarily for the working man or woman who has

* Received for publication July 10, 1931.

a job. Such people can pay for treatment, but cannot pay fees high enough to insure the best work. In order to strike a balance between running costs and the ability on the part of the clients to pay, and still pay the dentists an adequate amount, we took advantage of subsidies of various kinds. Administration costs were absorbed by the Industrial Clinic; the capital costs of $350 necessary to establish the work were borne by two interested industries; and space and a chair in the day dental clinic at the Montreal General Hospital, usually idle in the evening, were used from 7 to 9 P.M. In order that the clinic might function as a private one for various industries, it was arranged that these industries could be billed for services to their employees. They could then proceed to recover the amount as they saw fit, by deduction from wages. Some bore half the cost themselves and were thus able to give some dental attention to their employees without committing themselves to an investment of $3,000 or more for equipment which might prove unpopular and remain idle a large part of the time.

As its name implies, the clinic operates from 7 to 9 every evening except Saturdays, Sundays, and legal holidays. It is closed during the months of July and August.

Organization

The director of the Industrial Clinic is the administrative head of the organization, which is not incorporated. The funds of the clinic are kept in a savings bank account in the director's name, in trust. He receives the monies paid in for dental work and issues checks on the account to the dentists, the assistant, and the dental supply houses.

The appointment sheet is kept at the Industrial Clinic of the hospital during the day, and appointments may be made there by telephone. The books and accounts of the clinic are open to inspection and auditing at any time by any interested person, but this is the first financial statement made public.

The only nonprofessional employee of the organization is a young lady who gives two hours each evening to the work. She receives the patients, arranges future appointments, receives cash payments, makes out the accounts payable by the different firms, and gives chair-side assistance to the dentists. She also attends to the ordering of the necessary supplies. She received a weekly salary of $5 from the opening of the clinic in December, 1928, until March, 1929, $6 from then until November, 1929, and $7 up to June, 1930; from that time up to the present she has been receiving $7.50.

The dentists are paid on the basis of $2 an hour, or $4 an evening. At the present time one dentist comes on Monday and Friday evenings, one on Tuesday and Thursday, one on Wednesday and Friday, and a fourth on Wednesday only. Dentures are prepared by a dental mechanic by private arrangement.

Work Done and Scale of Fees

The dental work undertaken is limited to prophylaxis, fillings, extractions with local anesthetic, and the preparation of dentures. Inlays are done by special arrangement with the dentist performing the work. No attempt is made to do crown and bridge work. Patients who require multiple extractions with general anes-

thesia are sent to the day dental clinic at the hospital, and a fee of $5 is paid for them.

The following is an approximate scale of fees:

Amalgam fillings	
Simple	$1.50
Compound	2.50
Synthetic porcelain fillings	2.50
Pyorrhea treatments	1.00
Extractions with local anesthetic	.50
Dentures	
Single	15.00
Double	30.00
X-rays	
Single film	.50
Complete set	5.00

Prices are based on a rate of $4 for an hour occupied on a patient. A gradual reduction of fees was undertaken from the start, in order that receipts and expenditures might be approximately the same. Dentures were reduced to two for $25 during the second year and part of the third, but a rather serious deficit appearing in December, 1930, led us to increase the price to the regular figure.

Financial Statement

The following is an account of receipts and expenditures over the period of operation:

FIRST YEAR

DECEMBER 10, 1928, TO JUNE 30, 1929

Capital donated	$350.00	Expenditure of capital: Engine, motor, cabinet, instruments, supplies	$350.00
Receipts		*Expenditures*	
Proceeds of practice	$1,467.15	Dentists	$572.00
Bank interest	1.31	Assistant	160.08
		Technician	290.99
		Supplies	82.36
		Printing	24.00
		Orderly	5.00
			1,134.43
		Profit and balance for depreciation of instruments and depletion of supplies	334.03
	$1,468.46		$1,468.46

SECOND YEAR

SEPTEMBER 1, 1929, TO JUNE 30, 1930

Receipts		*Expenditures*	
Proceeds of practice	$2,112.35	Dentists	$1,049.00
Bank interest	6.54	Assistant	288.00
		Technician	421.20
		Supplies	232.78
		Printing	2.00
		Orderly	5.00
		Legal advice re general liability	15.00
			2,012.98
		Profit	105.91
	$2,118.89		$2,118.89

Add previous surplus, $334.03, to profit for this year, $105.91. Balance as of June 30, 1930 ..... $439.94

THIRD YEAR

SEPTEMBER 1, 1930, TO JUNE 30, 1931

Receipts		*Expenditures*	
Proceeds of practice	$2,085.40	Dentists	$1,132.00
Bank interest	4.41	Assistant	307.50
		Technician	443.80
		Supplies	230.78
		Printing	19.00
		Orderly	5.00
Loss	48.27		
	$2,138.08		$2,138.08

Deducting this loss of $48.27 from previous balance of $439.94, we arrive at the surplus of $391.67 for three years' operation.

The item "supplies" includes all renewal of instruments and materials, and the materials for making dentures supplied to the dental tehnician.

When we first proposed to organize this work, we could find no records of other similar ventures. We therefore publish this article in the hope that it will be of some service to those who may contemplate the establishment of a similar clinic in some city comparable to Montreal.

THE TOXICITY OF METHYL CHLORIDE FOR LABORATORY ANIMALS*

JOHN L. WHITE AND PAUL P. SOMERS

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TWENTY-NINE cases of poisoning by commercial methyl chloride gas, resulting in ten deaths within a period of one year, were reported in Chicago by Kegel, McNally, and Pope (1) in August, 1929. Investigation disclosed that in all but three of these cases a leak existed in an apartment refrigerator in which methyl chloride gas was used as a refrigerant. The three exceptions were exposed to the gas in other ways.

The possible danger from widespread use of this gas in domestic refrigerators called for more detailed study of its toxic properties. Recent experimental work by Sayers, Yant, and others of the United States Bureau of Mines (2) showed that concentrations of the gas as low as 0.12 to 0.15 per cent. are sufficient to produce death in guinea-pigs, with characteristic pathology. However, the periods of exposure of the animals in these experiments were relatively short, the longest exposure in the series being thirteen and one-half hours.

Inasmuch as the gas is odorless, and lacking in irritating properties, the possibility that a slow leak in a refrigerator might expose the occupants of an apartment to the action of the gas in a concentration which would be so low as to produce no immediate alarming effects, but which would in time cause death or serious injury to health, was considered.

In order to note the effects of long exposure to small concentrations of the gas, experiments were undertaken in the Bureau of Laboratories and Research for the purpose of determining the minimal concentration which would cause death in average-sized guinea-pigs when the exposure covered a period of three days.

The pigs were exposed, in series of three, to a mixture of methyl chloride gas and air in an incubator with base dimensions of 17 by $17\frac{1}{2}$ inches and an interior height of 25 inches. A wire shelf with a perforated pad 12 inches above the base of the compartment was used as a platform for the animals. The air and the methyl chloride gas were introduced into the incubator through openings in the side near the base. This arrangement permitted an intimate mixture of air and gas before it was breathed by the animals. The mixture of air and gas was withdrawn continuously, by a water suction line, through an outlet about 3 inches above the animal shelf, so that the mixture withdrawn was

* Read before the Laboratory Section of the Fifty-Ninth Annual Convention of the American Public Health Association, at Fort Worth, Texas, October, 1930.

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representative of the air being breathed by the guinea-pigs.

The rate of flow of the gas as it entered the chamber was determined by passing it through water and noting the rate of bubble formation. The suction pump was operated at a speed which would supply sufficient air to produce the desired concentration of methyl chloride in the mixture.

Carrots were placed in the chamber at the beginning of each test and were replenished every twenty-four hours. In supplying fresh carrots it was necessary to keep the door of the compartment open but a few seconds. The condition and behavior of the pigs during the time of exposure to the gas were observed through the inner glass door of the incubator.

Measured quantities of the gaseous contents of the chamber were drawn from the incubator at frequent intervals and the percentage of methyl chloride was determined by the combustion method of Martinek and Marti (3), in which the methyl chloride in the presence of a large excess of air is converted into hydrochloric acid, which in turn is absorbed by standard silver nitrate solution. The results were expressed as methyl chloride, in parts per million.

The animals were removed from the incubator after exposure, and were placed in wire cages and kept under observation for thirty days. Those that died during the course of the test were examined for pathologic changes. Control animals were subjected to all the conditions of the experiment, except exposure to the methyl chloride gas, and remained apparently healthy during the thirty days of observation.

Fifty-four guinea-pigs were exposed for seventy-two hours to average concentrations of from 49 to 140 parts of methyl chloride per million parts of air, or to percentages of from 0.0049 to 0.014. Table 1 gives in detail the concentrations of the gas and the effect on the animals. An analysis of this table discloses that the minimal toxic concentration of methyl chloride in air, for guinea-pigs when the period of exposure is seventy-two hours, is about 75 parts of the gas to a million parts of air, or 0.0075 per cent. At this concentration 50 per cent. of the pigs died. Concentrations of around 50 parts of methyl chloride per million parts of air failed to cause death in any of the eighteen pigs exposed, while concentrations around 140 parts of the gas per million parts of air regularly caused death, with typical pathology, within a few days after the exposure.

TABLE 1.—EFFECT OF SEVENTY-TWO HOURS' EXPOSURE OF GUINEA-PIGS TO VARYING CONCENTRATIONS OF METHYL CHLORIDE IN AIR

PARTS OF METHYL CHLORIDE PER MILLION PARTS OF AIR			NO. OF GUINEA-PIGS		
Lowest Reading	Highest Reading	Average Reading	Exposed	Released as Normal	Died
2	98	49 = 0.0049%	18	18	0
58	104	77 = 0.0077%	18	9	9
42	284	140 = 0.0140%	18	0	18

The pathologic findings in the animals which died indicated a wide-

spread systemic poisoning. The most constant finding was severe congestion of both lungs, accompanied by edema and hemorrhage. Blood tinged fluid was found occasionally in the pleural cavity. Congestion of the dura mater was noted in all the animals. Microscopic examination disclosed dilatation of the capillaries of the cerebrum and, in some instances, petechial hemorrhages. In addition to these findings, congestion of the liver, pancreas, adrenal cortex, kidneys, and intestines was noted, but these latter findings were not so constant as the changes noted in the meninges and the lungs. The heart was usually dilated, and there was congestion of the coronary blood vessels. Hemorrhages into the alimentary canal were not infrequent, for both stomach and intestinal contents were blood tinged in some instances. Microscopically, the kidneys showed degenerative changes in addition to petechial hemorrhages. The bladder at autopsy usually was distended with urine, the latter containing a large amount of albumin, with pus cells and granular casts. In general the pathologic picture was characteristic and corresponded to the findings of Sayers, Yant, and others in animals subjected to much higher concentrations for a shorter time.

The confusion of methyl chloride poisoning with food poisoning in some of the cases reported led to the consideration of the possibility of poisoning's resulting from the consumption of food exposed to methyl chloride gas. In order to investigate this possibility, carrots were exposed to a mixture of methyl chloride and air for a period of three days, and were then fed to guinea-pigs. Chemical analysis of the carrots showed traces of methyl chloride, but the guinea-pigs fed with them exhibited no symptoms of poisoning during the observation period of sixty days.

Conclusion

The minimal lethal concentration of methyl chloride gas in air for guinea-pigs exposed for seventy-two hours was found to be approximately 75 parts of methyl chloride per million parts of air, or 0.0075 per cent.

Carrots exposed to methyl chloride gas in air absorbed traces of methyl chloride but failed to produce symptoms of poisoning when fed to guinea-pigs.

The pathologic changes in guinea-pigs dying from the effects of extremely low concentrations of methyl chloride in air were characteristic, indicating severe circulatory disturbances. The most constant changes were congestion of the lungs and of the meninges.

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THE RÔLE OF PUNCTATE BASOPHILIA IN THE CONTROL OF INDUSTRIAL PLUMBISM*

RONALD E. LANE, M.B., B.S. (LOND.), M.R.C.P. (LOND.)

PUNCTATE basophilia in red blood cells was first described by Ehrlich (1) in 1885. Much was written on the subject during the next thirty years. In 1919 Pappenheim (2) summarized the literature and published detailed accounts of the nature of the change, of its causation, and of its relation to the other basophilic conditions. In 1924, Key (3) working with rabbits showed that the stippled cell is the young cell; and in 1928, Brookfield (4) confirmed these findings in the human subject. Most authorities are now agreed that the basophilic substance is of cytoplasmic origin; and the suggestions of Cooke (5) that it is the remains of the original cytoplasm of the erythroblast and that the reason for its taking the azur-eosin stain after fixation with alcohol may be found in a defect in the immature lipin covering, are attractive.

Punctate basophilia appears in a number of conditions, notably pernicious anemia, leukemia, cachexia following neoplasm, and in any secondary anemia. Lehmann (6) has also described the condition in cement workers. In none of these conditions is this phenomenon so frequently observed in such a marked degree as in lead poisoning. Behrend (7) was the first to note this association, as long ago as 1899, and since the beginning of the present century much has been contributed to the literature on this subject. In 1925, Sellers (8) showed how the degree of punctate basophilia could be used as a means of comparing the degree of absorption likely to arise in men working on various lead processes. The present contribution is on similar lines to Sellers' work and confirms many of his original conclusions.

During the past three years, over 4,000 punctate counts have been carried out upon workers engaged in the electric accumulator trade who are exposed to lead hazards of varying magnitude. An attempt has been made to assess their value as a means of detecting excessive absorption at an early stage—long before any clinical signs appear—since it was felt that if this were possible, an early modification of the process thus proved dangerous could be effected. In this way a preventive measure of considerable value would be available in the control of this widespread industrial disease.

Where practicable, the amount of lead in the atmosphere was also estimated, so that these two groups of findings could be correlated. The technic employed in these investigations is as follows:

Punctate Counts.—Blood is obtained from the lobe of the ear, and a thin film made on a glass slide. A hemoglobin estimation is

* Received for publication June 16, 1931.

also made as a routine at this stage. The film is fixed in absolute methyl alcohol and stained by Sellers' method; *i.e.*, the film is immersed in alkaline methylene blue for half a minute; it is then washed in tap water until it becomes a pale green color. It is blotted and dried, and examined under a one-twelfth inch oil immersion lens. In counting, about an hour and a quarter is devoted to each slide; 100 fields are carefully searched and the punctate cells found are noted, together with their type. In every tenth field, the number of red cells per field is estimated, using an Ehrlich eyepiece. In this way, some 12,000 to 20,000 red cells are carefully scrutinized. The final result is expressed as the number of punctate cells per million erythrocytes. The size of the granules is noted in each case. The actual counting is done by trained assistants, each slide being subsequently examined by the writer.

Determination of Lead in Atmosphere.—Air is drawn by an electric pump through a Gooch crucible packed with cotton wool (tight at the bottom and looser at the top), and then through an air meter. The crucible is fixed up at the point at which the determination is required, with its intake directed downward, and is protected by a large-mesh wire cage. It has been pointed out by Burstein (9) that it is important in any series that the same direction of intake should be maintained.

The collection of the sample goes on over about six hours, and some 3 to 400 cubic feet of air are drawn through the apparatus. At the end of the period, the cotton wool is carefully removed and the quantity of lead dust arrested is estimated by the following method and expressed as metallic lead per 10 cu.m.[1] The cotton wool is extracted with hydrochloric acid and bromine. The liquid is filtered off and evaporated nearly to dryness. Excess of ammonia is now added. The excess is then boiled off and the liquid filtered to remove the iron. The bulk of the filtrate is now made up to 100 c.c., of which 50 c.c. (or a convenient part) is boiled for five minutes with 2 c.c. of 0.1 normal sodium thiosulphate; 1 c.c. of 10 per cent. potassium cyanide solution is immediately added and then 10 c.c. of ammonia of 0.88 specific gravity. This is then boiled for ten minutes, cooled, washed into a 100-c.c. Nessler glass, and made up to 50 c.c.; 50 c.c. of 0.5 per cent. gelatine solution is added and then one drop of ammonium sulphide, and the whole is thoroughly mixed. The color obtained is matched by treating a blank exactly as described above and using a standard solution of lead sulphate, 1 c.c. of which contains 0.1 mg. of lead.

In order properly to appreciate the significance of the findings here presented, something should be known of the appearance of normal blood when stained by this method. With this object in view, blood films were taken from 223 normal subjects; the results are shown in Table 1. Groups were taken from London and from Manchester; and medical students were compared with manual workers, because it was discovered early that there was some difference in the findings in these groups. The figures in the Manchester cases were in each instance rather higher than those in the London cases; and the manual workers gave a slightly higher figure than the students. From these observations we may conclude that punctate basophilia, as demonstrated by this method of staining, is to be observed in a definite, if minor, degree among normal members of the population with no industrial exposure.

Kehoe (10) in America, Badham and Taylor (11) in Australia, and Francis (12, pp. 24 and 25) in Great Britain have each demonstrated the presence of lead in the urine of normal persons, showing that lead is normally absorbed by most of us; and it is just conceivable that this punctate baso-

[1] I am indebted to Mr. R. T. Harrison for carrying out the estimations.

philia among normal subjects is due to lead absorption of a very minor degree.

The lead worker naturally absorbs more lead than the normal person. It must, however, be stressed that lead absorption is not synonymous with lead poisoning. In most of us, and certainly in all lead workers, lead is being absorbed and excreted. A state of equilibrium exists, and provided the dosage is kept within certain limits, no harm is demonstrable. The limits of this dosage will be discussed more fully in a future paper. It is only intended here to show the relation between punctate basophilia and exposure to varying lead hazards. Some evidence of this relationship is afforded by the findings presented in Table 2, where the quantity of lead in the urine is also shown. The number of subjects in the groups examined is, however, very small indeed;

TABLE 1.—RESULTS OF EXAMINATION OF BLOOD FILMS OF 223 NORMAL SUBJECTS WITH NO KNOWN EXPOSURE TO LEAD

PUNCTATE BASOPHILS PER MILLION RED BLOOD CELLS	MANCHESTER SUBJECTS		LONDON SUBJECTS	
	No.	Per Cent.	No.	Per Cent.
Manual Workers				
Free	40	40.0	28	50.9
100–1,000	43	43.0	20	36.4
1,000–2,000	15	15.0	6	10.9
Over 2,000	2	2.0	1	1.8
Total	100	100.0	55	100.0
Students				
Free	20	66.7	34	89.5
100–1,000	7	23.3	4	10.5
1,000–2,000	3	10.0	0	0.0
Over 2,000	0	0.0	0	0.0
Total	30	100.0	38	100.0

TABLE 2.—RELATION BETWEEN PUNCTATE BASOPHILIA AND EXPOSURE TO VARYING LEAD HAZARDS[1]

NO. OF MEN IN GROUP	PUNCTATE BASOPHILS PER MILLION RED BLOOD CELLS	LEAD IN URINE		LEAD IN AIR
		Per Liter	In 24 Hours	
		mg.	*mg.*	*mg. per 10 cu.m.*
7	6,400 S.M.L.[2]	0.36	0.46	3.0
4	4,400 S.M.	0.22	0.26	2.5
4	1,600 S.	0.06	0.09	0.8

[1] None of the men in these groups showed any other sign or symptom of lead poisoning.
[2] S = small granules; M = medium; and L = large.

consequently the results have little statistical value, but they are, nevertheless, of considerable interest. I am indebted to the Chairman of the Departmental Committee on Ethyl Petrol for permission to use the figures for lead in urine which were obtained for that Committee by Mr. Francis.

In Tables 3, 4, and 5, results are presented which show the value of punctate counts among groups of lead workers.

TABLE 3.—RESULT OF IMPROVING WORKING CONDITIONS

NO.	DECEMBER, 1927		DECEMBER, 1929	
	Punctate Basophils per Million Red Blood Cells	Lead in Air	Punctate Basophils per Million Red Blood Cells	Lead in Air
		mg. per 10 cu.m.		*mg. per 10 cu.m.*
1[1]	13,200 S.M.L.		...	
2	6,100 S.M.L.	11 determinations	2,400 S.M.	12 determinations
3	1,500 S.M.		...	
4	5,700 S.M.L.	5.4	4,000 S.	1.9
5[2]	27,100 S.M.L.	4.7	...	2.4
6	12,100 S.M.	4.2	1,100 S.	2.8
7	4,500 S.M.L.	3.5	1,200 S.	1.6
8[1]	11,000 S.M.L.	4.4	1,900 S.	1.9
9	4,000 S.M.	4.3	...	2.0
10[2]	32,300 S.M.L.	8.8	...	2.5
11[1]	10,500 S.M.L.	5.3	...	1.4
12	4,300 S.M.	7.1	800 S.	2.8
13	6,100 S.M.	3.6	2,100 S.	1.2
14	6,600 S.M.L.	7.7	6,000 S.	1.7
15	5,500 S.M.L.		1,400 S.M.	1.1
16	7,100 S.M.		2,400 S.	
17	5,000 S.M.L.		...	
18	6,100 S.M.L.		1,500 S.	
19[2]	44,800 S.M.L.		...	
20	3,100 S.M.L.		...	
21	...		3,800 S.	
22	...		2,300 S.	
23	...		600 S.	
24	...		1,600 S.	
25	...		2,400 S.	
26	...		3,500 S.M.	
27	...		2,100 S.	
28	...		500 S.	
29	...		Free	
Average.....	10,800 S.M.L.	5.4	2,100 S.	1.9

[1] Case of mild plumbism with debility.
[2] Case of clinical plumbism with colic.

Table 3 shows the counts obtained from twenty men, in December, 1927. At this time, the conditions under which they were working were very

unsatisfactory, and three cases of clinical plumbism occurred (all characterized by colic and constipation, with general debility). It will be seen that the mean figure for lead in the general atmosphere was 5.4 mg. per 10 cu. m. The punctate counts determined at this time were correspondingly high and the average count for this group was 10,800. Small, medium, and large granules were present in practically every case. Very extensive alterations in the method of removing the dust were made; and two years later, the lead in the general atmosphere was found to have fallen to 1.9 mg. per 10 cu. m. This drop in the lead contamination of the atmosphere was reflected in the blood condition of the men; it will be seen that the average punctate count fell to 2,100. Small and very fine granules only were found. This figure represents a minimum of lead absorption, and is not greatly in excess of that found among the normal subjects. The determinations of lead in air here quoted have a definite comparative value, although their absolute value is probably not great.

Legge and Goadby (13) have suggested as a safe limit that the air *breathed* should not contain more than 5 mg. per 10 cu.m.; in order to insure this, however, our experience would indicate that the *general atmosphere* should not contain more than 2 mg. This is accounted for by the facts that most of the dust is produced in the immediate neighborhood of the worker by his work or by the movement of his clothing, and that if a figure of 5 mg. is allowed for the general atmosphere then the actual air breathed will contain considerably more. There are other factors, however, to be considered in this connection, and these will be dealt with more fully in a future paper.

TABLE 4.—RESULT OF REDUCING LEAD EXPOSURE BY HALF

	PUNCTATE BASOPHILS PER MILLION RED BLOOD CELLS		
	October, 1928 Before Change	April, 1929 Immediately before Change	November, 1929 Six Months after Change
Average for all men working at process at time of sampling[1]	6,000 S.M.	5,800 S.M.	1,500 S.
Average for all men working at process who were present for each sampling (13 men)	6,000 S.M.	5,800 S.M.	2,500 S.

[1] In October and April, 16 men were employed; in November, 32.

Table 4 shows the results obtained by reducing the lead exposure in a group of men by half. These men are engaged on a form of lead burning, and in October, 1928, showed a mean count of 6,000; small and medium granules were found. Six months later, another series of counts was made which gave an average of 5,800. Immediately after this, the work was reduced by half; *i.e.*, the men worked

alternate weeks at lead burning and on nonhazardous work; and in October, 1929, the average count was 1,500. In three cases this alteration was not made, and the counts in these men remained stationary.

Table 5 is interesting as an example of the useful purpose served by punctate counts in anticipating trouble. In January, 1928, the average counts of all the men employed on this process was 10,600 small, medium, and large granules. These men had been working under these conditions for upwards of two years; seven complained of no untoward symptoms and only one showed a blue line. Changes were made which included a reduction of the time spent on the work by half, and a compulsory daily bath, together with a complete change of clothing and underclothing for use during working hours. Counts were made each month, and three months later the average count had dropped to 2,600; small and medium granules were present. Several volunteered the fact that they felt more fit and in better health than previously—although they had never complained. The monthly count some months later had risen to 7,000 (small, medium, and large granules); and it was obvious that for some reason the men were again absorbing too much lead. Investigations were made and it was eventually found that some of the main trunking of the local exhaust ventilation plant was partially blocked. This was remedied and three months later the mean count had fallen to 2,500 (small and medium granules), around which figure it has now remained for approximately two years.

TABLE 5.—AVERAGE NUMBER OF PUNCTATE BASOPHILS PER MILLION RED BLOOD CELLS IN A GROUP OF ELEVEN MEN[1]

DATE	PUNCTATE BASOPHILS PER MILLION RED BLOOD CELLS
Jan., 1928	10,600 S.M.L.
April, 1928	2,600 S.M. (3 mos. after change)
July, 1928	7,000 S.M.L. (trunking discovered defective)
Oct., 1928	2,500 S.M.
Oct., 1929	2,100 S.

[1] Eight were present throughout; three were not present for first sampling.

Size of Granules

Sellers (14) has remarked upon the different types of granules found and on their varying significance. Cooke (15) has shown that he can produce any type of granule by varying the treatment of the blood; but in all our work, a constant procedure has been adhered to and the importance of the size of the granules must be stressed. In this series, the type of punctate basophilia has in every case been noted, and the stippling classified as very fine, small, medium, or large. Cooke (5) again has pointed out the

difficulty in distinguishing between punctate basophilia and granular polychromasia. Care has always been taken to distinguish between these as far as possible; and cells showing the hazy and ill-defined granules have been classed as polychromes. The two conditions merge, however, and differentiation presents difficulty in a few cases. The classification has always been decided upon by the acuteness of definition of the granules, no matter what their size.

The very fine and the small granules are seen in those normal subjects who show punctate basophilia, and in practically all lead workers. These are the cells which are easily missed unless the films are well prepared and the person making the count is experienced. One might here stress the care which must be taken with the methyl alcohol used for fixation, if unreliable results are to be avoided.

Mathew (16) says that in his work many of the finely stippled cells were missed. This is quite sufficient to account for the fact that our figures are on a higher scale than his. It is the type of cell showing this form of stippling which appears in increasing numbers on slight or moderate exposure to lead. If the exposure is slight, no other type is likely to appear. If, on the other hand, it is moderate in degree, medium granules appear after a month or two of exposure and usually persist while this exposure is maintained. A few months after it ceases, they usually disappear, leaving only the small and the very fine granules which persist, though in decreasing numbers, for several months further. The presence of large granules is usually an indication of excessive and rapid absorption, and is therefore a sign of great importance.

Discussion

The value of punctate basophilia to the physician called upon to deal with lead workers can be discussed under two heads: (1) diagnosis and (2) prophylaxis.

Diagnosis.—Great care is necessary here. The mere presence of punctate basophilia is not enough on which to diagnose lead poisoning; it is merely, as has been demonstrated, an indication, if present in a marked degree, of recent absorption of lead. The actual count in different individuals varies; and the time that has elapsed since the last exposure is of great importance. In fact, the longer a worker has been away from his work, the less the value of the count; six months after exposure it is, in most cases, practically valueless. The complete absence of punctate basophilia in three samples taken within a week of exposure and while acute symptoms are complained of, is strong but not absolutely conclusive evidence against a diagnosis of plumbism. The presence of a marked punctate basophilia with large granules, together with such other changes in the blood picture as a fall in hemoglobin, changes in shape and size of red cells, and increase in number of polychromes, is strong confirmatory evidence for a diagnosis of plumbism. Beyond this one cannot go. Small granule counts up to 3,000 are of little or no significance in a lead worker; they merely indicate that he is a lead worker. In making a diagnosis of lead poisoning, great stress must be laid upon the symptoms and the clinical picture, which

should be considered in conjunction with the complete blood picture.

Prophylaxis.—The really great help to be obtained from punctate basophilia is in this connection. As has been demonstrated, the average count of a group of workers and the tendency of that count to rise or fall are of much greater significance than individual counts; by the aid of such counts processes can be controlled and a watch kept upon whole departments. A steady tendency to rise in the count of any group of workers must call for immediate action; and investigations must be made until the cause of the increase has been located and rectified.

As an aid to detecting the worker who is especially susceptible to lead, the punctate count is again useful. In a new employee put to work on a process, the hazard of which is known, an unusual and rapid rise in the count, especially if associated with a fall in the hemoglobin content during the first few weeks of work, indicates that the man is either particularly careless or unduly susceptible. In either case, he is unsuitable for lead work.

Conclusions

1. Punctate basophilia, as demonstrated by Sellers' method of staining, was present in a minor degree in approximately half of 223 normal subjects examined.
2. Punctate basophilia on a more extensive scale is present in practically all workers exposed to a lead hazard.
3. A quantitative estimation of the punctate basophilia is desirable and great stress must be laid upon the size of the granules. Large granules have a greater significance than small ones and denote excessive absorption or mobilization of lead.
4. The value of punctate counts in the diagnosis of plumbism is limited.
5. Punctate counts are of extreme value in the prophylaxis of plumbism among lead workers and are essential in the adequate hygienic control of lead processes.

I am indebted to the Chloride Electrical Storage Company, Limited, Manchester, for whom this work was carried out, for their permission to publish it.

I should like to record my gratitude to Dr. W. E. Cooke and Dr. A. Sellers for helpful criticism and advice.

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QUANTITATIVE MEASUREMENTS OF THE INHALATION, RETENTION, AND EXHALATION OF DUSTS AND FUMES BY MAN: II. CONCENTRATIONS BELOW 50 MG. PER CUBIC METER*

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INTRODUCTION

IN the first paper (1) of this series, Drinker, Thomson, and Finn showed that man at rest retains 55 per cent. of dust or fumes from inspired air containing from 50 to 450 mg. per cubic meter. The purpose of the present study was to determine the percentage of dust or fume retained at concentrations less than 50 mg. per cubic meter.

APPARATUS AND PROCEDURE

In general, the methods and apparatus used in both studies were the same. The dust or fume for inhalation was generated in a large dust cabinet (2) and its concentration in the air was determined at various intervals during the day. The results were plotted against time to give a settling curve (3) from which the concentration at any time could be read. The subjects inhaled from the dust cabinet and exhaled through an electric precipitator (4) into a large spirometer. A diagram of the apparatus is shown in Figure 1. The dust or fume was removed from the expired air by the electric precipitator and was then quantitated by chemical titration. The resulting value for dust in expired air was subtracted from the corresponding value for dust in inspired air, to give the amount of dust retained.

The differences in the apparatus in the two studies were unimportant. In the present study a 500 liter instead of a 125 liter spirometer was used for measuring air volumes. A mask, Heidbrink No. 21, covering the nose and mouth only was found to be more comfortable than the Kops type, which covers the whole face. Magnesium oxide was used as the fume for inhalation instead of zinc oxide because it is less toxic (5) and is easier to quantitate chemically.

The procedures in the two studies differed in several details. In the present study, the calcium carbonate dust used by Drinker, Thomson, and Finn (1) was dissolved in 0.1 N hydrochloric acid and titrated directly with 0.1 N alkali, whereas previously it was converted to calcium oxide, redissolved in hydrochloric acid, and then titrated with 0.01 N alkali. At the high concentrations studied by the previous investigators (1), sufficiently large amounts of dust and fume settled in the apparatus to necessitate cor-

* From a thesis presented to the Department of Sanitary Engineering, Harvard Engineering School, as partial fulfilment of the requirements for the degree of Doctor of Science.

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rection for this factor. In the present study, however, settlement of dust in the apparatus was found to be negligible.

In addition to breathing normally at rest, as in the former study (1), the subjects breathed dusty air by mouth while seated, and normally while exercising and also while inhaling approximately 5 per cent. carbon dioxide mixed with the dusty air. In mouth breathing the subject's nostrils were plugged with cotton. In normal breathing the subject breathed as he wished, generally by nose but probably occasionally by both nose and mouth, especially while exercising and while breathing carbon dioxide. Mouth breathing is generally abnormal in dusty air; one's natural reaction is to breathe by nose. The exercise was very moderate and by no means caused vigorous breathing or panting.

In this study, all air volumes were corrected to 21°C. (70°F.). No correction was made for temperature in the previous study, but unpublished data showed that the room temperature was between 70° and 80°F. In all probability, variations in barometric pressure from 760 mm. were not sufficient to influence the results of either study.

Experiments and Results

Data relating to the thirty-two subjects employed, together with the number and distribution of the experiments performed, are presented in Table 1. The essential data obtained from each experiment included the following: volume of air breathed; length of breathing period (usually fifteen minutes); milligrams of dust expired; room temperature; concentration of dust in inspired air; and respirations per minute. From these data, the values were calculated for concentration of dust in expired air, amount of dust retained, minute-volume of air breathed, and volume per respiration.

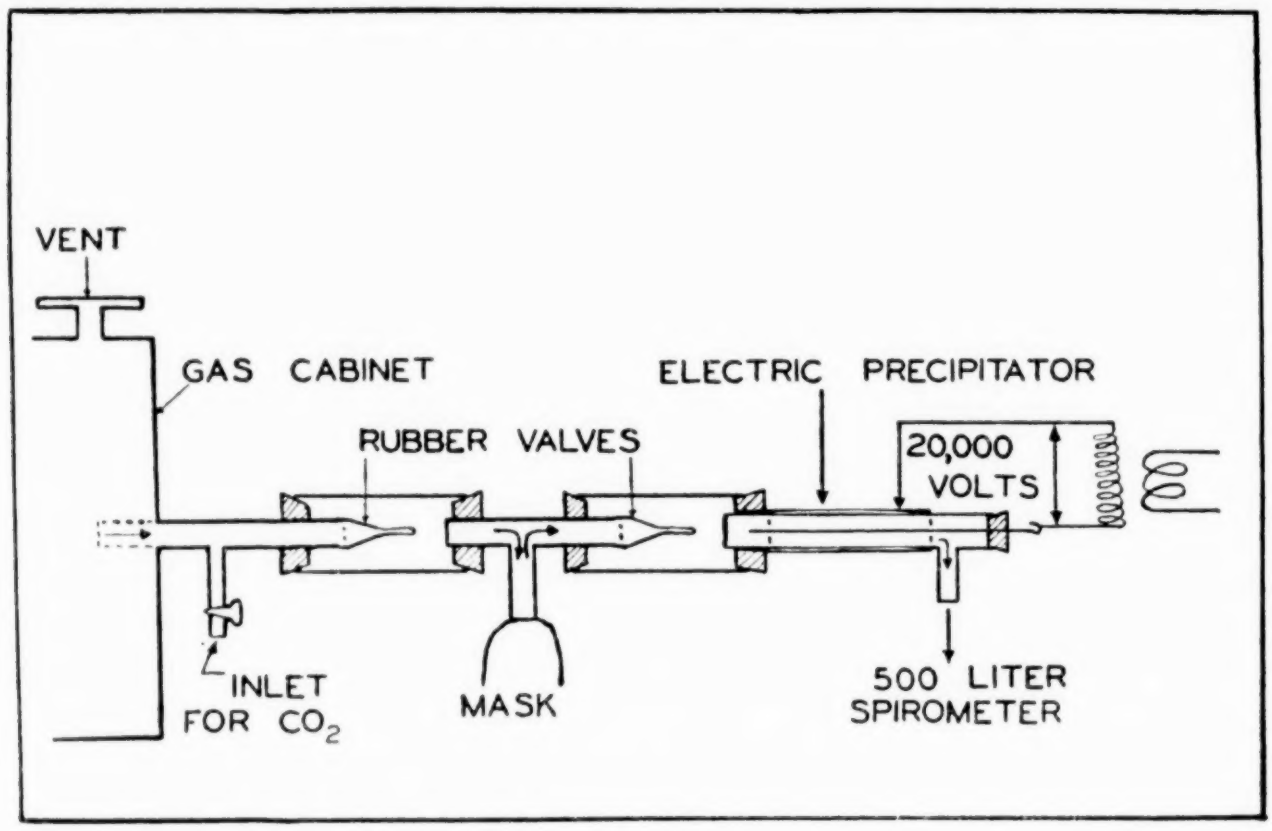

Fig. 1.—Apparatus used for determining the retention of inhaled dust by man.

TABLE 1.—STATISTICS OF SUBJECTS AND OF EXPERIMENTS

SUBJECT	AGE	WEIGHT	VITAL CAPACITY	DUST INHALED	NO. OF BREATHING EXPERIMENTS				
					Resting			Exercising	TOTAL
					Normal	Mouth	Normal 5% CO_2	Normal	
	yrs.	*lbs.*	*l.*						
1	36	160	6.1	MgO	9	2	..	..	11
2	26	135	4.0	"	30	9	11	9	59
				$CaCO_3$	6	3	2	5	16
3	24	165	5.3	MgO	6	..	..	..	6
4	32	165	4.0	"	1	..	..	..	1
5[1]	29	115	3.2	"	9	9	11	1	30
				$CaCO_3$	7	2	..	..	9
6	29	130	4.3	MgO	5	1	..	..	6
7	26	148	5.3	"	32	4	8	..	44
8	27	150	4.9	"	30	5	5	1	41
				$CaCO_3$	5	..	1	..	6
9	27	125	4.2	MgO	5	2	3	..	10
				$CaCO_3$	1	3	1	1	6
10	32	190	6.0	MgO	2	..	..	..	2
11	29	150	4.0	"	2	..	..	..	2
12	28	134	4.8	"	2	..	..	..	2
13[1]	29	138	3.8	"	1	..	..	..	1
14	23	165	5.6	"	3	..	..	..	3
15	41	145	4.8	"	1	..	..	..	1
16	22	158	4.9	"	5	..	..	..	5
17	21	142	4.8	"	9	2	..	..	11
18[1]	24	102	3.1	"	3	..	..	..	3
19	22	130	5.0	"	3	3	..	..	6
20[1]	48	162	2.0	"	2	2	3	..	7
21	34	139	4.3	"	...	..	1	..	1
22[1]	15	105	2.9	"	4	2	4	..	10
23	16	117	3.5	"	5	3	5	..	13
24[1]	..	....	....	"	8	5	9	..	22
25[1]	35	100	3.0	"	2	1	2	..	5
26[1]	25	128	3.0	"	1	1	1	..	3
27	64	150	1.7	"	1	1	1	..	3
28	41	157	3.1	"	1	1	1	..	3
				$CaCO_3$	8	4	5	3	20
29	22	118	3.6	MgO	..	..	..	3	3
30	26	155	5.6	"	1	1	..	16	18
31	31	140	4.0	"	1	1	..	16	18
32	16	....	3.7	"	1	1	..	13	15
Totals.....				MgO.....	185	56	65	59	365
				$CaCO_3$ ...	27	12	9	9	57
					212	68	74	68	422

[1] Female.

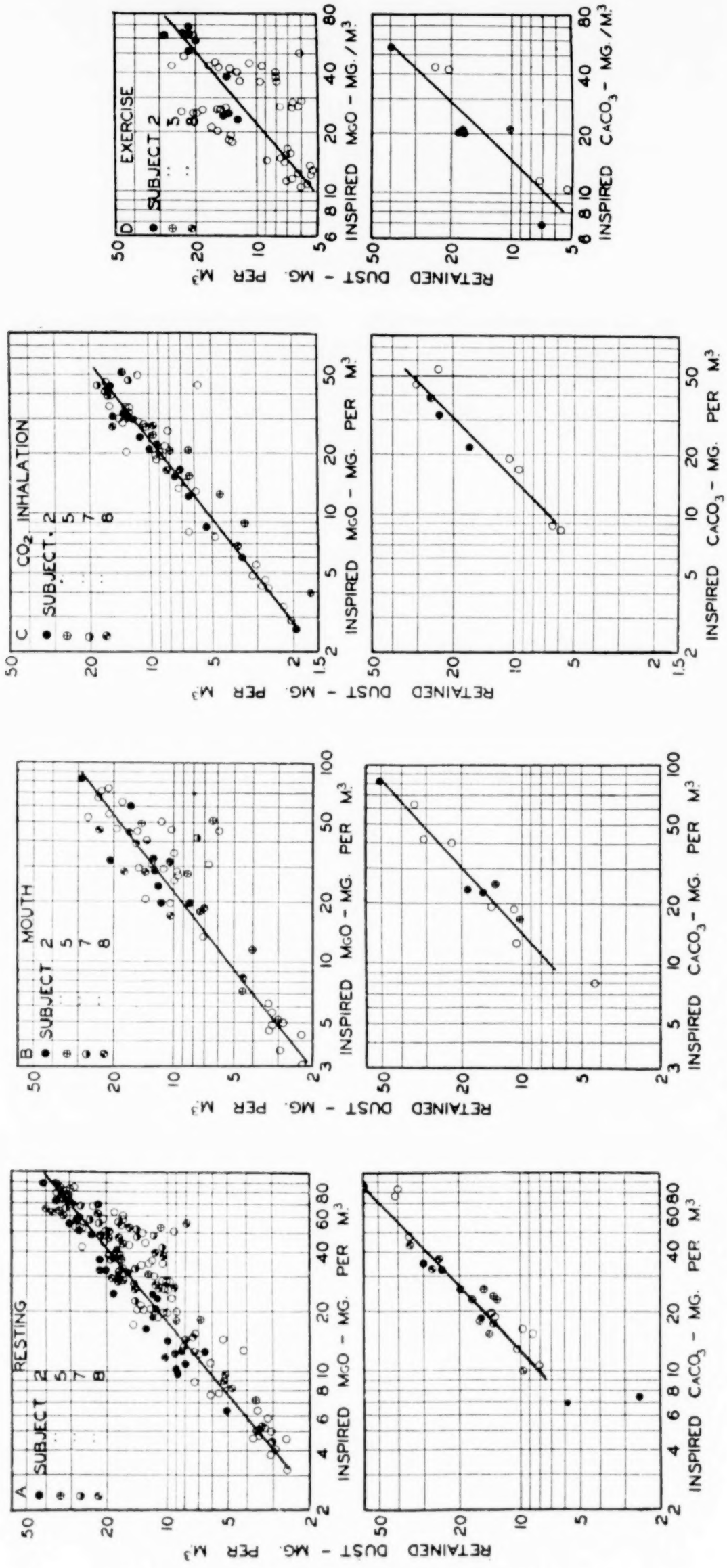
A RESTING
B MOUTH
C CO_2 INHALATION
D EXERCISE
SUBJECT 2 5 7 8
RETAINED DUST - MG. PER M.³
INSPIRED MgO - MG. PER M.³
INSPIRED $CaCO_3$ - MG. PER M.³

FIG. 2.—Magnesium oxide and calcium carbonate retained by subjects breathing under the indicated conditions.

The result obtained by plotting the amount of dust retained against the concentration of dust in the inspired air is shown in Figure 2. On double logarithmic paper the points fell into zones that could be represented by straight lines. Since these lines were straight over the dust concentration range studied—about 3 to 80 mg. per cubic meter—probably the lines could be extended in either direction with reasonable accuracy.

The dispersion of the experimental points about the fitted lines will be observed in Figure 2. An estimate of the influence of errors in experimental technic upon this scattering was obtained from an analysis of the difference in percentage retention between pairs of consecutive results determined under similar experimental conditions. For this study, only those pairs of consecutive results were chosen which represented observations on the same dust and the same subject, and which showed a difference in dust concentration not greater than 2.5 mg. per cubic meter, and a difference in respiration rate of not more than 2 per minute. These restrictions were met by fifty-two pairs of observations, involving eighteen different subjects and including data on both magnesium oxide and calcium carbonate and on the four breathing conditions employed in this investigation. The respiration rates varied from 5 to 29 a minute, and the concentrations of dust in inspired air from 4.2 to 81.3 mg. per cubic meter. For each pair of determinations the value of the second percentage retention was subtracted from the first. The results were arranged in an ordinary frequency table and the summation values plotted on arithmetic probability paper (6), as shown in Figure 3.

According to this curve, the median (50 per cent. value) difference between the second and the first determinations was −0.8 per cent., and the

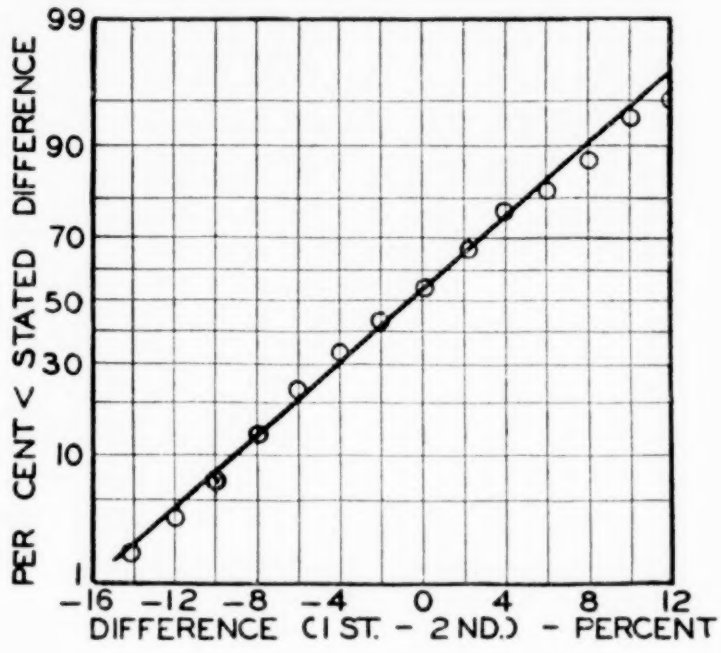

FIG. 3.—Frequency curve of differences between percentage retention results in the first and the second experiments of pairs of consecutive determinations.

probable error (75 per cent. minus 50 per cent. value) was ±4.5 per cent. These results show that on the average, the second determination did not differ significantly from the first, and that for one-half of the observations the difference did not exceed ±4.5 per cent. Thus, it may be concluded that errors in experimental technic caused little if any of the dispersion of the points about the fitted lines, noted in Figure 2. The variations may be explained in part in the light of certain measurable conditions which will be considered in the next paper of this series.

Percentage retention, Figure 4, was calculated from the fitted lines in Figure 2. The percentage of calcium carbonate retained during normal breathing while at rest varied from

about 80 per cent. at a concentration of 10 mg. per cubic meter to 70 per cent. at 50 mg. per cubic meter. The percentage of magnesium oxide retained under the same conditions varied from about 60 per cent. at 10 mg. per cubic meter to 45 per cent. at 50 mg. per cubic meter. Probably the difference of approximately 20 per cent. in the retention of these two materials was due to variation in the physical properties of the two substances. The percentage retention of dust at concentrations above 50 mg. per cubic meter changed but little; at concentrations below 10 mg. the increase in percentage retained with decrease in dust concentration was quite marked. Apparently, as the dust concentration approached zero, the percentage retention approached 100.

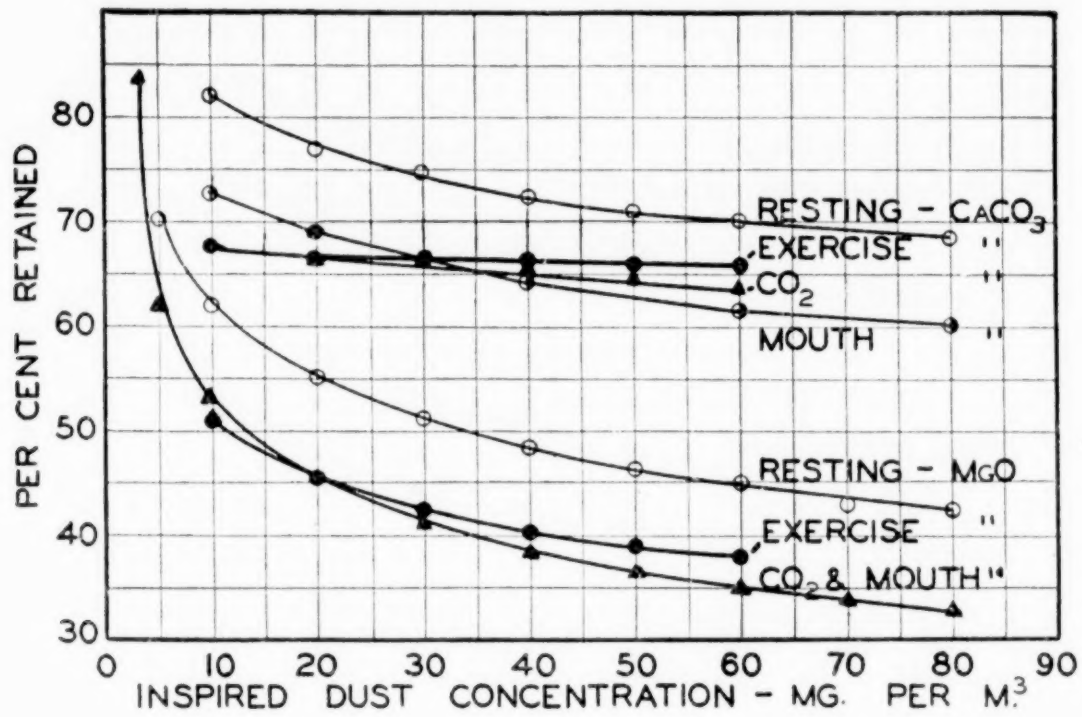

FIG. 4.—Percentage retention curves calculated from the fitted lines in Figure 2.

TABLE 2.—PERCENTAGE DUST RETENTIONS IN PRESENT EXPERIMENTS AND IN DRINKER'S EXPERIMENTS

DUST	CONCENTRATION	MINUTE-VOLUME AT 21°C. AND 760 MM.	RESPIRATIONS	RETENTION	INVESTIGATOR
	mg./cu.m.	*l.*	*no./min.*	%	
MgO	10– 50	10.5	17	60–45	Brown
ZnO (fume)	50–450	10.4	10	55	Drinker *et al.*
ZnO (Kadox)	50–450	10.4	11	55	Drinker *et al.*
$CaCO_3$	10– 50	10.5	17	80–70	Brown
$CaCO_3$	50–450	10.4	12	55	Drinker *et al.*

For each dust studied, the percentage retention was about 10 per cent. greater for normal breathing while at rest than for mouth breathing while resting, or for normal breathing during exercise or during the inhalation of approximately 5 per cent. carbon dioxide mixed with the dusty air (Fig. 4).

A difference in the character (rate and depth) of respiration was probably responsible for the decreased percentage retention during exercise and during carbon dioxide inhalation.

Percentage retention results from the former study (1), and the conditions under which they were obtained, were tabulated with data for the corresponding breathing condition (normal breathing while at rest) from the present study, and are shown in Table 2. The results from the two studies apply to average breathing conditions; they cannot be combined or compared, however, until the effect upon percentage retention of the conditions wherein they differ, notably in respiration rate, has been determined.

Summary

Four hundred and twenty-two experiments on the retention of magnesium oxide fume and of calcium carbonate (marble) dust by thirty-two subjects breathing normally while at rest, through the mouth while resting, and normally during exercise and during the inhalation of approximately 5 per cent. carbon dioxide in the air gave the following results:

The percentage of magnesium oxide retained during normal breathing while at rest varied from about 60 per cent. at a concentration of 10 mg. per cubic meter to 45 per cent. at 50 mg. per cubic meter. The percentage of calcium carbonate retained under the same breathing conditions varied from about 80 per cent. at 10 mg. per cubic meter to 70 per cent. at 50 mg. per cubic meter.

The percentage retention for mouth breathing while at rest and for normal breathing during exercise and during carbon dioxide inhalation was about 10 per cent. less than for normal breathing while at rest under the same conditions.

The percentage retention changed but little at concentrations above 50 mg. per cubic meter, but apparently rapidly approached 100 per cent. as the concentrations fell below 10 mg. per cubic meter.

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OCCUPATION AND HEALTH. ENCYCLOPAEDIA OF HYGIENE, PATHOLOGY AND SOCIAL WELFARE. Volume I. Paper. Pp. 999 with illustrations. Geneva: International Labour Office, 1930.[1]

The first volume of this new encyclopedia carries one from A through H. It is the work of ninety-five collaborators and necessarily displays great unevenness in the quality of the material presented. An encyclopedia covering a subject which begins to contain a certain amount of exact scientific information and which must develop by the accumulation of much more data of the same sort can function as little more than the starting point in any real inquiry. In the main, the articles contained in this first volume perform this service satisfactorily, and they usually leave the reader with bibliographic suggestions which can carry him further.

Occasionally one finds statements from European authors widely out of accord with American experience and practice, as for example the advocacy of blood transfusion and lobelin as therapeutic measures in treating carbon monoxide asphyxia. But doubtless a European reviewer would be equally disturbed by some of the presentations from this side of the Atlantic. Whether the International Labour Office will be able to provide the revisions which will be necessary to keep the encyclopedia actively in use is a question purchasers must necessarily ask. The present volume should have reasonable reliability for at least five years, and after some such lapse of time will gradually become a useful addition to the history of industrial hygiene and somewhat of a liability to the practice of this speciality.

The tenor of the work is nonmedical and, where possible, technical medical discussions have been avoided.—*Cecil K. Drinker.*

[1] The American agents for publications of the International Labour Office are the World Peace Foundation, 40 Mt. Vernon St., Boston, Mass.

SCHÄDLICHE GASE: DÄMPFE, NEBEL, RAUCH- UND STAUBARTEN. Von *Ferdinand Flury* und *Franz Zernik*, Würzburg. Mit autorisierter Benutzung des Werkes: Noxious Gases von Henderson und Haggard. Paper. Pp. XII, 637 with index and illustrations. Berlin: Julius Springer, 1931.

This most excellent book of reference should be found in all industrial libraries. It is essentially a translation and amplification of the valuable book, "Noxious Gases," by Henderson and Haggard, and is issued by the German authors in collaboration with their American predecessors in this important field of hygiene and medicine.

The work is thorough but not distressingly ponderous, and carries at the close of each section an excellently selected bibliography, so that the reader may readily go farther afield if he has necessity to do so.

The reviewer finds room for criticism in but one particular—the brevity of the index. In a volume essentially for quick reference this feature should be more extensive, and undoubtedly it will be improved in future editions.—*Cecil K. Drinker.*